

# WEST Search History

DATE: Monday, April 29, 2002

**Set Name Query**  
side by side

**Hit Count Set Name**  
result set

*DB=USPT,DWPI; PLUR=YES; OP=ADJ*

L1	balaban-d\$.in.	46	L1
L2	L1 and (probe near array)	9	L2
L3	probe near array or probe array	1780	L3
L4	exon and probe	5750	L4
L5	probe near5 (array or chip)	7891	L5
L6	join\$3 near5 (sequeunc\$ or junction)	9683	L6
L7	first exon and second exon	374	L7
L8	tiling or interrogat\$	37066	L8
L9	RNA or transcript\$ or alternative splic\$	59379	L9
L10	(RNA or transcript\$) and alternative splic\$	1809	L10
L11	immobiliz\$ near substrate	1175	L11
L12	join\$ near5 sequenc\$	6550	L12
L13	probes per centimeter square	0	L13
L14	l3 and l4	139	L14
L15	L14 and l5	139	L15
L16	L15 and l6	3	L16
L17	L15 and l7	1	L17
L18	L15 and l8	35	L18
L19	L18 and l9	35	L19
L20	L18 and l10	9	L20
L21	L15 and l10	18	L21
L22	L21 and l11	0	L22
L23	L15 and l11	6	L23
L24	L23 and l12	2	L24
L25	set near2 probe	4710	L25
L26	L25 and l4 and l5 and l6 and l8 and l9 and l20 and l11	0	L26
L27	l25 and l7	8	L27
L28	L27 and l5	0	L28
L29	l4 and l5 and l8	54	L29
L30	L29 and l10 and l11	0	L30
L31	L11 and l8	46	L31
L32	L31 and l5	27	L32

=> d his

(FILE 'HOME' ENTERED AT 12:13:27 ON 27 JUN 2001)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'  
ENTERED AT 12:13:43 ON 27 JUN 2001

L1 155 S BALABAN D?/AU  
L2 1 S L1 AND PROBE AND ARRAY  
L3 0 S L1 AND EXON AND PROBE  
L4 0 S L1 AND ALTERNATIVE SPLICING  
L5 1980 S PROBE (10A) (ARRAY OR CHIP)  
L6 3 S TILING AND L5  
L7 0 S L5 AND ALTERNAT? (5A) SPLIC?  
L8 30 S L5 AND (EXON#)  
L9 0 S L8 AND (JOIN? (5A) SEQUENC? OR JUNCTION)  
L10 245825 S (JOIN? (5A) SEQUENC? OR JUNCTION)  
L11 41 S L10 AND L5  
L12 24 DUP REM L11 (17 DUPLICATES REMOVED)  
L13 2 S L12 AND (EXON# OR RNA OR TRANSCRIPT? OR ALTERNATIVE SPLIC?)  
L14 0 S L12 AND (TILING OR INTERROGAT?)  
L15 2 S L6 AND (EXON# OR RNA OR TRANSCRIPT? OR ALTERNATIVE SPLIC?)  
L16 0 S L12 AND (EXON#)  
L17 41125 S ALTERNATIVE (3A) SPLIC?  
L18 8042 S L17 AND EXON AND MRNA  
L19 0 S L18 AND L5  
L20 702 S L18 AND PROBE#  
L21 3 S L20 AND (ARRAY OR CHIP)

=>

END OF SEARCH HISTORY

**WEST**

Generate Collection

L27: Entry 1 of 7

File: USPT

May 8, 2001

DOCUMENT-IDENTIFIER: US 6228639 B1

TITLE: Vectors and methods for the mutagenesis of mammalian genes

## DEPR:

The retroviral vectors are highly mutagenic. One significant advantage provided by the present retroviral vectors is the fact that these vectors are highly mutagenic. This property arises, at least in part, because the vectors contain a combination of a consensus splice acceptor and transcriptional termination sequences. The splice acceptor has been previously described (Gossler et al., Science 244:463-465 (1989); Friedrich and Soriano, Genes Dev. 5:1513-1523 (1991); Skames et al., Genes Dev. 6:903-918 (1992); Takeuchi et al., Genes Dev. 9:1211-1222 (1995); Wurst et al., Genetics 139:889-899 (1995); Forrester et al., Proc. Natl. Acad. Sci. USA 93:1677-1682 (1996); and Brenner et al., Proc. Natl. Acad. Sci. USA 86:5517-5521 (1989)), but the combination with termination sequences is novel, and this combination is important for the elimination of read-through transcription which is frequently observed in cellular sequences flanking proviruses (Swain and Coffin, Science 255:841-845 (1992)). The termination sequence also enhances mutagenicity by blocking potential bypassing of the insertion by alternative splicing mechanisms which make use of fortuitous chromosomal splice sites; these sites are inaccessible due to transcription termination at t.

## DEPR:

Alternatively, detection of a retroviral integration site may be accomplished by direct sequencing of the amplified DNA of an ES clone; this approach, however, requires the isolation of single clones of ES cells and is preferably used only for a subset of the generated clones. In another alternative approach, an integration site may be determined by sequence detection using a positional oligonucleotide probing technique (POP), a method which is ideal for the processing of limited sequence information in parallel. According to this technique, all possible oligonucleotides of a specific length are synthesized in a high density array (such as an Affymetrix chip (see, for example, Lipshutz et al., BioTechniques 19:442-447 (1995)) and hybridized to the amplified DNA from ES cells. The POP technique is based on generating sequence information for an unknown region of nucleic acid (i.e., the genomic DNA), which is linked to a known sequence (i.e., a portion of the retroviral vector). Because retroviral integration is precise and results in the integration of a viral LTR within the genomic DNA, the LTR sequence is a preferred sequence for designing oligonucleotide probes. For example, oligonucleotides that contain 8 bases corresponding to the tip of the LTR and nine random bases can probe  $4e9=262,144$  combinations. This strategy of junction sequencing by oligonucleotide arrays can be used in place of, or in parallel with, the hybridization technique described above. As information about the mouse genome sequence increases, this sequence tag approach will become increasingly useful in identifying insertions in known genes.

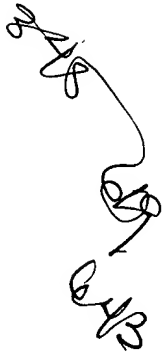
## ORPL:

Lipshutz et al., "Using Oligonucleotide Probe Arrays to Access Genetic Diversity," BioTechniques 19(3):442-447 (1995).

## ORPL:

Robberson et al., "Exon Definition May Facilitate Splice Site Selection in RNAs and Multiple Exons," Molecular and Cellular Biology 10(1):84-94 (1990).

L2 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1999-04520 BIOTECHDS  
TI Computer-readable storage media with stored relational database;  
for storing information relating to polymer **probe** arrays  
used for DNA sequence study  
AU **Balaban D J**; Hubbel E A; Mittman M; Cheyng G; Dai J  
PA Affymetrix  
LO Santa Clara, CA, USA.  
PI WO 9905574 4 Feb 1999  
AI WO 1998-US15456 24 Jul 1998  
PRAI US 1997-69436 11 Dec 1997; US 1997-53842 25 Jul 1997  
DT Patent  
LA English  
OS WPI: 1999-143157 [12]  
AB A computer-readable storage medium, on which the following relational  
database is stored, is claimed. The relational database comprises a  
**probe** record table, in which each **probe** record  
specifies a polymer **probe** for use in a **probe**  
**array**, and a sequence item table including records specifying  
respective nucleotide sequences to be studied in the **probe**  
**array**, there being a many-to-many relationship between the  
**probe** records and the sequence item records. Also claimed are: a  
computer-implemented method for operating a relational database; and a  
computer system with a processor for accessing the above storage medium.  
The method is used for storing and organizing information relating to  
polymer e.g. DNA **probe array** DNA chips, including  
oligonucleotide **array** chips, useful in expression analysis, DNA  
polymorphism analysis, etc. The storage medium can store and organize  
large amounts of information interrelating probes on a chip, genomic  
items investigated by the chip and sequence information relating to chip  
design, using a database model, which is readily translated into  
database  
language such as SQL. (35pp)  
CC A GENETIC ENGINEERING AND FERMENTATION; A1 Nucleic Acid Technology  
CT COMPUTER-READABLE STORAGE MEDIUM, STORED RELATIONAL DATABASE, APPL.  
OLIGONUCLEOTIDE DNA **PROBE ARRAY**, DNA CHIP, DNA  
POLYMORPHISM ANALYSIS BIOCHIP HYBRIDIZATION (VOL.18, NO.9)



=>



Experimental annotation of the human genome using  
microarray technology.

AUTHOR: Shoemaker D D; Schadt E E; Armour C D; He Y D;  
Garrett-Engle P; McDonagh P D; Loerch P M; Leonardson A;  
Lum P Y; Cavet G; Wu L F; Altschuler S J; Edwards S; King  
J; Tsang J S; Schimmack G; Schelter J M; Koch J; Ziman M;  
Marton M J; Li B; Cundiff P; Ward T; Castle J; Krolewski  
M;  
Meyer M R; Mao M; Burchard J; Kidd M J; Dai H; Phillips J  
W; Linsley P S; Stoughton R; Scherer S; Boguski M S

CORPORATE SOURCE: Rosetta Inpharmatics, Inc., Kirkland, Washington 98034,  
USA.

SOURCE: NATURE, (2001 Feb 15) 409 (6822) 922-7.  
Journal code: NSC; 0410462. ISSN: 0028-0836.

PUB. COUNTRY: England: United Kingdom  
(EVALUATION STUDIES)  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200103

ENTRY DATE: Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered PubMed: 20010309  
Entered Medline: 20010322

AB The most important product of the sequencing of a genome is a complete,  
accurate catalogue of genes and their products, primarily messenger RNA  
transcripts and their cognate proteins. Such a catalogue cannot be  
constructed by computational annotation alone; it requires experimental  
validation on a genome scale. Using 'exon' and 'tiling' arrays  
fabricated by ink-jet oligonucleotide synthesis, we devised an  
experimental approach to validate and refine computational gene  
predictions and define full-length transcripts on the basis of  
co-regulated expression of their exons. These methods can provide more  
accurate gene numbers and allow the detection of mRNA splice  
variants and identification of the tissue- and disease-specific  
conditions  
under which genes are expressed. We apply our technique to chromosome 22q  
under 69 experimental condition pairs, and to the entire human genome  
under two experimental conditions. We discuss implications for more  
comprehensive, consistent and reliable genome annotation, more efficient,  
full-length complementary DNA cloning strategies and application to  
complex diseases.

CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:493727 CAPLUS

DOCUMENT NUMBER: 129:118762

TITLE: Analysis of genetic polymorphisms and gene copy  
number

INVENTOR(S): using oligonucleotide probe arrays  
Cronin, Maureen T.; Miyada, Charles G.; Hubbell, Earl  
A.; Chee, Mark; Fodor, Stephen P. A.; Huang, Xiaohua  
C.; Lipshutz, Robert J.; Lobban, Peter E.; Morris,  
Macdonald S.; Sheldon, Edward L.

PATENT ASSIGNEE(S): Affymetrix, Inc., USA  
SOURCE: PCT Int. Appl., 114 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830883	A2	19980716	WO 1998-US6414	19980102
WO 9830883	A3	19981029		

W: JP, US  
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 970251 A2 20000112 EP 1998-947218 19980102  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1997-778794 19970103  
WO 1998-US6414 19980102

AB The invention provides methods for detecting variations in polymorphic sites and/or variations in gene copy no. A no. of strategies for comparing a polynucleotide of known sequence (a ref. sequence) with variants of that sequence (target sequence) are provided. The comparison can be performed at the level of entire genomes, chromosomes, genes, exons or introns, or can focus on individual mutant sites and immediately adjacent bases. The strategies allow detection of variations, such as mutations or polymorphisms, in the target sequence irrespectively of whether a particular variant has previously been characterized. The strategies both define the nature of a variant and identify its location in a target sequence. The strategies employ arrays of oligonucleotide probes immobilized to a solid support (DNA chips). Target sequences are analyzed by detg. the extent of hybridization at particular probes in the array. The strategy in selection of probes facilitates distinction between perfectly matched probes and probes showing single-base or other degrees of mismatches. The strategies usually entails sampling each nucleotide of interest in a target sequence several times, thereby achieving a high degree of confidence in its identity. This level of confidence is further increased by sampling of adjacent nucleotides in the target sequence to nucleotides of interest. The present tiling strategies result in sequencing and comparison methods suitable for routine large-scale practice with a high degree of confidence in the sequence output. The methods are particularly useful for anal. of biotransformation genes, such as cytochromes P 450, and for screening an animal to tissue for the



capacity to metabolize a drug.

pooled. Positive hybridizations may be assigned to the probes selected to check particular DNA segments because these segments usually differ in 75% of their constituent bases.

Brief Summary Paragraph Right (22):

By using a larger set of longer probes, longer targets may be conveniently analyzed. These targets may represent pools of shorter fragments such as pools of exon clones.

Brief Summary Paragraph Right (23):

A specific hybridization scoring method may be employed to define the presence of heterozygotes (sequence variants) in a genomic segment to be sequenced from a diploid chromosomal set. Two variations are where: i) the sequence from one chromosome represents a basic type and the sequence from the other represents a new variant; or, ii) both chromosomes contain new, but different variants. In the first case, the scanning step designed to map changes gives a maximal signal difference of two-fold at the heterozygotic position. In the second case, there is no masking, but a more complicated selection of the probes for the subsequent rounds of hybridizations may be indicated.

Brief Summary Paragraph Right (24):

Scoring two-fold signal differences required in the first case may be achieved efficiently by comparing corresponding signals with controls containing only the basic sequence type and with the signals from other analyzed samples. This approach allows determination of a relative reduction in the hybridization signal for each particular probe in a given sample. This is significant because hybridization efficiency may vary more than two-fold for a particular probe hybridized with different DNA fragments having the same full match target. In addition, heterozygotic sites may affect more than one probe depending upon the number of oligonucleotide probes. Decrease of the signal for two to four consecutive probes produces a more significant indication of heterozygotic sites. Results may be checked by testing with small sets of selected probes among which one or few probes selected to give a full match signal which is on average eight-fold stronger than the signals coming from mismatch-containing duplexes.

Brief Summary Paragraph Right (25):

Partitioned membranes allow a very flexible organization of experiments to accommodate relatively larger numbers of samples representing a given sequence type, or many different types of samples represented with relatively small number of samples. A range of 4-256 samples can be handled with particular efficiency. Subarrays within this range of numbers of dots may be designed to match the configuration and size of standard multiwell plates used for storing and labelling oligonucleotides. The size of the subarrays may be adjusted for different number of samples, or a few standard subarray sizes may be used. If all samples of a type do not fit in one subarray, additional subarrays or membranes may be used and processed with the same probes. In addition, by adjusting the number of replicas for each subarray, the time for completion of identification or sequencing process may be varied.

Brief Summary Paragraph Right (28):

In Format 3, a first set of oligonucleotide probes of known sequence is immobilized on a solid support under conditions which permit them to hybridize with nucleic acids having respectively complementary sequences. A labeled, second set of oligonucleotide probes is provided in solution. Both within the sets and between the sets the probes may be of the same length or of different lengths. A nucleic acid to be sequenced or intermediate fragments thereof may be applied to the first set of probes in double-stranded form (especially where a recA protein is present to permit hybridization under non-denaturing conditions), or in single-stranded form and under conditions which permit hybrids of different degrees of complementarity (for example, under conditions which discriminate between full match and one base pair mismatch hybrids). The nucleic acid to be sequenced or intermediate fragments thereof may be applied to the first set of probes before, after or simultaneously with the second set of probes. A ligase or other means of causing chemical bond formation between adjacent, but not between nonadjacent, probes may be applied before, after or simultaneously with the second set of probes. After permitting adjacent probes to be chemically bonded, fragments and probes which are not immobilized to the surface by chemical bonding to a member of the first set of probe are washed away, for example,